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February 1956

Disease-a-Month

Obesity

WILLIAM PARSON
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Disease-a-Month Series

MONTHLY CLINICAL MONOGRAPHS ON CURRENT MEDICAL PROBLEMS

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CONTENTS

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OBESITY is a current and lively problem. The medical profession has become aware that the obese individual is not in the optimal state of health and that he is, in fact, threatened with decreased life expectancy because of increased susceptibility to the "degenerative disorders" and other diseases. The general public, as well, has shown considerable interest in this problem. Obesity has become a fashionable subject for newspaper and magazine articles, books, advertising campaigns, even comic strips. Dietary programs, beauty courses and "reducing pills" are widely advertised. As a result the sophisticated patient no longer hides behind "it must be my glands, because I don't eat anything, doctor"; rather, he wonders about the role of emotional difficulties in relation to his obesity. "Is there something to take that will control the appetite? Is there any virtue to the fancy diets?"

The patient asks these questions. And the physician asks himself many more: Why do people get fat? Why, for that matter,

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doesn't everyone get fat? Why is it so hard for fat people to get thin? And why is it so much harder for them to stay thin?

In this presentation, it is proposed to bring into focus the problems involved in understanding and treating the patient who is obese. The available facts will be supplemented by reasonable hypotheses and a working approach will be offered.

THE DEFINITION OF OBESITY
or What Should I Weigh?

All reasonable men would agree that a man is obese who weighs too much because he has accumulated too much fat. Naturally, the question arises, how much fat is "enough." Obviously there is no categorical answer. The percentage of fat or labile body tissue may vary tremendously depending upon the state of nutrition. It may vary from only 5 per cent of the body weight in profound undernutrition to 70 per cent or more in the extremely obese person (1, 2). Intensive efforts are under way in a number of centers to appraise the fat content of the body, but this valuable measurement is not easily accomplished (1, 3). Four methods have been outlined as possible ways to determine the percentage of fat: (1) measurement of the total body water; (2) accurate measurement of skin folds; (3) dilution technic using fat-soluble indicators; (4) determination of body density or specific gravity.

The densitometric method has been most widely used and is probably the most accurate method available at the present time.

This method is based on the fact that human fat has a density of 0.92 and the rest of the body, the lean body mass, has a density of 1.1. It is possible to calculate the percentage of fat when the body specific gravity is known. The essential measurement in this method is that of body volume. This is determined by hydrostatic weighing to get the equivalent volume which is equal to weight in air minus the weight in water. Body specific gravity is obtained from the ratio of body weight to that of equivalent volume. The percentage of fat is then determined from Behnke's formula (3).

$$\% \text{ Fat} = 100 \frac{5.548}{\text{sp. gr.}} - 5.044$$

The difficulty is that this method requires the weighing of the subject under water, which is tedious and time consuming, thus limiting its use mainly to clinical research.

The measurement of skin fold thickness is the simplest to carry out but has been thought to be the least accurate. Body fat is determined by an empiric formula based on the measurement of skin fold thickness over several specific areas of the body. A recent report (4) utilizing a type of caliper which is more accurate may increase the value of this method.

The total body water method depends upon the principle that the water content of the lean body mass is approximately 73 per cent. Under normal conditions total body water is maintained in a constant relationship to the lean body mass. If the total body water is determined, then the lean body mass can be calculated and the fat content of the body determined by subtracting the lean body mass from the total body weight. Total body water measurements have been time consuming, and expensive, and as a result have not been widely used. A new method using radioactive iodine-labeled iodoantipyrine (5) looks promising as a simple and quick method to determine total body water.

The percentage of fat or the corollary the "lean body mass" would be very desirable to obtain in many metabolic studies. The latter has been shown to be a better reference point for physiologic processes than the commonly used measurements (6). A very interesting point regarding obesity has been shown by these studies in that there is an increase in body fat with age even though the total weight remains the same (1).

These studies should prove to be extremely useful in establishing the range of fat content at various ages for both sexes. One day an informative reference standard may be available for appraisal of variation from the "normal" fat content of a patient. Perhaps then, the factors involved in control of the size of the fat deposits in the normal individual will be understood.

At present the best available "weight standard" is based on the healthiest body weight, or the weight with the best life expectancy. This introduces in a clear fashion the point, to be discussed later, that it is unhealthy to be overweight.

The most desirable weight for an individual is most reasonably estimated from use of the standard weight table with proper al-

XUM

IDEAL WEIGHT FOR ADULTS (METROPOLITAN LIFE INSURANCE CO.)

Height, with Shoes		MEN*			Height, with Shoes		WOMEN*		
		Small Frame	Medium Frame	Large Frame			Small Frame	Medium Frame	Large Frame
Ft.	In.				Ft.	In.			
5	2	116–125	124–133	131–141	4	11	104–111	110–118	117–127
5	3	119–128	127–136	133–144	5	0	105–113	112–120	119–129
5	4	122–132	130–140	137–149	5	1	107–115	114–122	121–131
5	5	126–136	134–144	141–153	5	2	110–118	117–125	124–135
5	6	129–139	134–147	145–157	5	3	113–121	120–128	127–135
5	7	133–143	141–151	149–162	5	4	116–125	124–132	131–142
5	8	136–147	145–156	153–166	5	5	119–128	127–135	133–145
5	9	140–151	149–160	157–170	5	6	123–132	130–140	138–150
5	10	144–155	153–164	161–175	5	7	126–136	134–144	142–154
5	11	148–159	157–168	165–180	5	8	129–139	137–147	145–158
6	0	152–164	161–173	169–185	5	9	133–143	141–151	149–162
6	1	157–169	166–178	174–190	5	10	136–147	145–155	152–166
6	2	163–175	171–184	179–196	5	11	139–150	148–158	155–169
6	3	168–180	176–189	184–202					

*Weight in pounds (as ordinarily dressed).

lowance for frame size and muscular development (see Tables). It is widely recognized that cultural and esthetic factors set the pattern for the "stylish figure." In practice, the use of a full length mirror may be the determinant of the patient's goal. Occasionally this raises a special problem when an apparently unrealistic "defatted" figure is sought.

THE NATURE OF ADIPOSE TISSUE
or What Does Fat Do for Me?

Fat may act as a cushion or an insulator or, in proper location and proportion, it may be esthetically pleasing; however, the principal function of fat in the body is to provide a large reserve of food or available energy. The capacity to store protein and carbohydrate is extremely limited; the capacity to store fat is almost unlimited. It can be stored in an almost pure state and has a greater caloric value than an equal weight of carbohydrate

or protein. Recent studies showed that the caloric value of labile body tissue in obese subjects was approximately 2.5 calories per gram (7). This would indicate that a considerable amount of water is stored and released as part of the caloric response, since the combustion of 1 Gm. of fat in the pure state releases approximately 9 calories.

Adipose tissue was considered for many years to be metabolically inactive. This view is no longer tenable in view of recent investigations, and it is now considered to be in the dynamic state (8). The deposition and mobilization of fat in adipose tissue is an active metabolic process. Adipose tissue is supplied by a dense capillary network and innervated by the autonomic nervous system. Synthesis of new fatty acids, the transformation of one fatty acid to another and the synthesis of glycogen all appear to take place in adipose tissue (8). All of these metabolic functions are influenced by nervous and endocrine factors.

This is perhaps getting a little ahead of the story; however, it seems clear that there is no evidence at the present time that the adipose tissue of the obese patient differs from that of a normal person. It can be mobilized and used as a source of energy when there is a "caloric deficit" (9). There is no convincing evidence that lipogenesis in an obese patient differs from the normal except in quantity.

THE HAZARDS OF OBESITY
or What If I Do Gain Weight?

The expense of life insurance gives some indication of the hazards of obesity. It is a well established clinical doctrine that the overweight patient is a "poor risk" almost regardless of the nature of the underlying disorder. And despite the lack of clear understanding of the pathogenesis, it has long been felt that obesity plays a part in the casuality of a number of diseases, including diabetes and the so-called degenerative disorders.

Statistics have been accumulated by the insurance companies in dealing with overweight clients (10–12). It appears that a decrease in life expectancy may be correlated with the degree of obesity within certain limits. The threat to survival affects young adults as well as the more aged (Fig. 1). Diseases which

present an increased hazard to the obese have been tabulated in terms of incidence in relation to the non-obese (Fig. 2).

It is interesting to speculate concerning the role of obesity in the pathogenesis of diabetes. The relative insulin insufficiency which characterizes this disorder may result from a number of morbid processes. It seems clear that insulin plays an essential

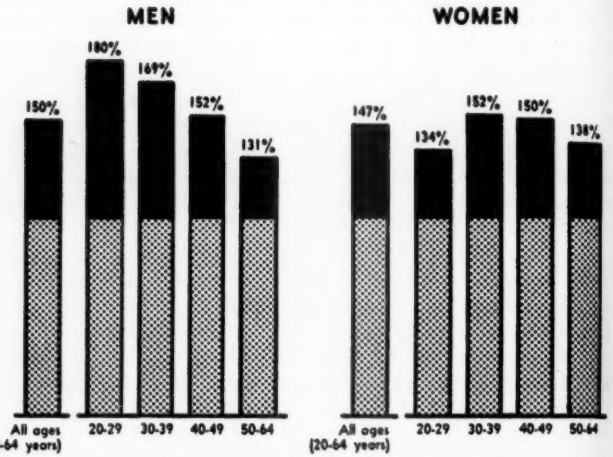

FIG. 1.—Effect of obesity on death rates at various age levels; based on mortality of individual uprated for overweight compared to expected deaths by mortality experience on standard risks. (Figs. 1–3: Metropolitan Life Insurance Co.; Dublin, L. I., and Marks, H. H.: Tr. A. Life Insur. M. Dir. America 35:235, 1952.)

role in lipogenesis. There has been a renewed interest in lipogenesis in the last few years, mainly due to the discovery and the elucidation of the role of coenzyme A (CoA) in fat metabolism (13,14). It is now well established that carbohydrate is converted into fat primarily by way of pyruvate, which is subsequently decarboxylated to form acetyl CoA. It is clear that acetyl CoA is the major precursor of long chain fatty acids. The first major metabolic process involved in the conversion of carbohydrate to fat is therefore glycolysis, which in turn is insulin dependent. It follows that any substance which can give rise to acetyl CoA or

XUM

"active acetate" can be converted to fatty acids. A number of tissues, including adipose tissue itself, have the ability to synthesize fat (8). In the absence of insulin, fat formation from the two carbon precursors, the ubiquitous "active acetate," is inhibited. It is undoubtedly too naive to suppose that excessive fat formation tends to "exhaust the insulin mechanism"; however, there is surely a clue herein.

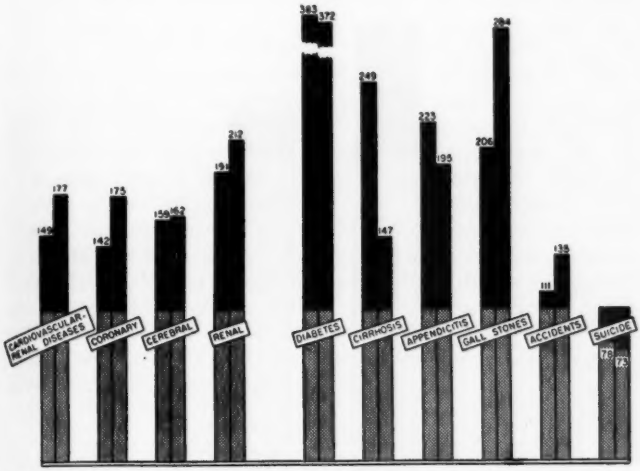

FIG. 2.—The effect of obesity on death rates in various diseases. *Left,* females; *right,* males. Based on analysis of principal causes of death among men uprated for overweight compared to estimated standard risks.

The pathogenesis of atherosclerosis is being studied intensively. It is suggested that activity of this process is related to alterations in the plasma content of various lipids. In turn it is possible that similar abnormalities are associated with the presence of obesity. The mechanisms are far from clear, but the suspicion is great that atheroma formation is encouraged by fat formation.

It is obvious that leanness is desirable for longevity. It would also seem that the excessive sweating, breathlessness with minor exertion, difficulty in walking and unattractiveness would also be an incentive to lose weight.

REVERSIBILITY OF MORBID PROCESSES ASSOCIATED WITH OBESITY

or What Good Will It Do Me to Reduce?

The question is not often raised, although it is a critical one, as to whether the decreased life expectancy of the obese individual is ameliorated when the excess fat is lost. Actuarial figures

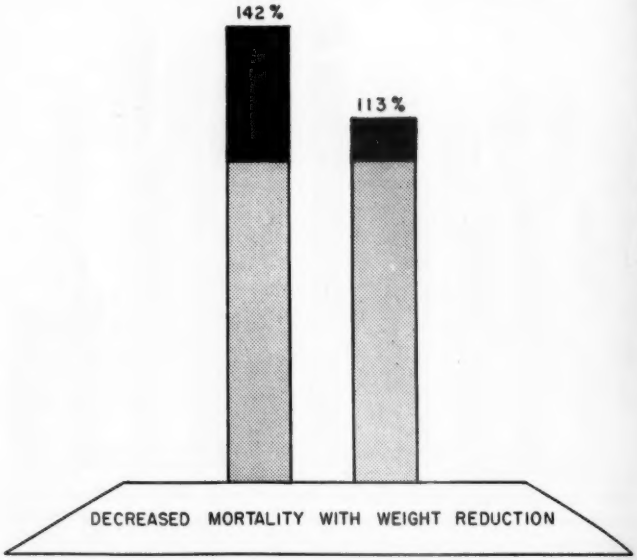

FIG. 3.—Over-all figures for both sexes and all ages of mortality of persons uprated for overweight who later received lower ratings after weight reduction, compared with mortality of all cases in original rating class.

offer comfort in this regard. Although the technics are open to criticism, studies have been made of insurees who have dieted to normal after having previously been "uprated" for obesity. It appears that the life expectancy is returned toward normal (Fig. 3). Short term studies of numbers of reduced "obese diabetics" have shown a return to normal of the glucose tolerance curves.

Similarly, short term studies of reduced "obese hypertensives" have shown fairly consistent declines in blood pressure.

A word of caution regarding the interpretation of these studies. We are dealing with two morbid processes, hypertension and obesity, their etiologies are unknown. The fact that weight reduction is associated with a reduction in blood pressure does not prove a direct relationship. There may be a third factor, the removal of which causes both weight reduction and a lowering of blood pressure. A recent study (15) does cast some doubt on a direct relationship between obesity and hypertension. Long term studies of these two groups would be of considerable interest.

Parenthetically it should be noted that there is a paucity of prognostic studies on long term sustained weight reduction, because long term "cures" of obesity are rarely reported.

Further support for the "benefits in longevity" of weight reduction comes from reports of the decreased occurrence of deaths due to degenerative vascular disease in countries during periods of relative famine, with subsequent rebounds in their incidence when food becomes abundant again. There is even suggestive necropsy evidence of reversibility of atheromatous lesions in subjects who have lost considerable weight before death (16).

It is unnecessary to list the obvious benefits of correction of the mechanical liabilities of obesity.

REVIEW OF FACTORS INFLUENCING FOOD INTAKE
or Why Doesn't Everybody Get Fat?

There are several aphorisms in the obesity literature. If more calories are consumed than are utilized for tissue repair, growth and energy expenditure, fat will be stored. If fewer calories are consumed than are utilized for tissue repair, growth and energy expenditure, fat stores will be depleted. No one will argue this. Nor is there sound evidence to argue the premise that there is any abnormality in the obese which permits increased efficiency of absorption, transport or metabolism of nutrients which would favor fat deposition.

It is proper to assume that the homeostatic mechanisms of the body tend to match the food intake to the body needs. The constancy of body weight in the "normal" person attests to this.

XUM

The man who is gaining weight and storing fat is in disequilibrium: his food intake is not in balance with his body requirements.

Before considering possible sites of such a disturbance, it is of interest to review certain features of the normal mechanisms.

It has been clearly established by precise localization of electrolytic lesions and stimulating electrodes in the hypothalamus of many animal species that there are bilaterally located "feeding centers" in this area of the central nervous system (17). Studies have shown that stimulation of one of the laterally located pair of nuclei results in marked increase of food ingestion, whereas bilateral destruction of these nuclei will result in rejection of food even to the point of starvation to death. Destruction of the pair of medial nuclei results in hyperphagia. To date, attempts to alter the eating pattern by stimulation of the latter nuclei have not been successful.

The more lateral areas have been related to "food drive" and the more medial areas have been termed "satiety centers." According to Brobeck (18), these hypothalamic mechanisms do not represent the most basic mechanisms of feeding behavior, which must be reflex in nature, as the hypothalamus is too high in the brain stem to represent a really fundamental neural circuit.

The lateral nuclei facilitate the eating reflexes and the medial nuclei inhibit them, either directly or through an inhibitory effect on the lateral nuclei. The feeding reflexes (perhaps via the hypothalamic mechanism) are undoubtedly affected by a host of neural connections with cortical, gustatory, olfactory, visual and other areas. The experimental observations have been so consistent in the many animal species that despite the lack of human studies the general concept has been applied to thinking about the process in man.

Hunger has been defined as the state of discomfort resulting from food deprivation and relieved by the ingestion of food. Pioneer studies relating the hunger state to vigorous gastric contractions have been nullified in part by observations of persistent hunger sensations in man variously gastrectomized, vagotomized and splanchnicectomized. It is not clear whether the increased gastric contractions represent a manifestation of food deprivation (by mechanisms as yet unexplained) or whether they might result from the following sequence: (1) food depriva-

tion → (2) "altered metabolism" → (3) increased activity of lateral hypothalamic nuclei → (4) facilitation of eating behavior. In animals this state is characterized by increased running as well as pawing, licking, swallowing, etc. Perhaps increased motility of the gastrointestinal tract fits into this pattern. On the other hand, "hunger contractions" may contribute to the facilitation of eating behavior.

Food ingestion may reverse the foregoing sequence: (1) food ingestion → (2) "altered metabolism" → (3) increased activity of medial hypothalamic nuclei (satiety center) → (4) inhibition of lateral hypothalamic nuclei (food drive center) → (5) inhibition of eating behavior. As already stated, step (3) may lead directly to step (5). Also, the mechanical effect of food in the gastrointestinal tract may augment this sequence.

Hunger, by definition, emphasizes the discomfort associated with food lack; appetite, in contrast, may be defined in terms of a pleasurable anticipation of food, or a desire for food which, from experience, is known to be "satisfying." In man, with his superior learning capacity, it is to be expected that learned responses will influence the eating reflexes considerably more than in lower animals.

In the sequences outlined earlier an essential step is labeled "altered metabolism." This phrase refers to the change in blood constituents or tissue metabolism related to the states of food ingestion and food deprivation. It is assumed that the medial hypothalamic nuclei (satiety center) is responsive to the former, and the lateral hypothalamic nuclei (food drive center) is responsive to the latter.

No blood constituent has as yet passed the vigorous test of showing proper inverse correlation with the hunger and satiety states in health or disease. Mayer's glucostatic theory (19) gets around many of the obvious objections to the role of the blood sugar as the critical constituent. It is postulated that the critical factor is the rate of glucose utilization by the tissues; possibly the movement of glucose or potassium or phosphates into the proper hypothalamic nuclei triggers the sequence outlined above. Evidence, which is controverted (20), has been offered as indirect support in the form of large blood peripheral glucose arteriovenous differences (indicating an increased rate of glucose utiliza-

XUM

tion) during satiety and diminished glucose A-V differences (decreased rate of glucose utilization) during the hunger state. This evidence is much too indirect, for studies of rates of glucose utilization by the brain show no significant alterations while peripheral glucose A-V differences are widening and narrowing after meals.

This problem remains to be resolved. However, there is recent direct evidence that the hypothalamic feeding centers show special sensitivity to the hunger state. It has shown that these centers in the rat take up more radioactivity (administered as radioactive glucose, phosphate or carbonate) in the starved than in the fed state (21). This behavior in the starved state is unique to this area, for contiguous hypothalamic areas and other zones in the brain show evidence of greater radioactive uptake following feeding than during starvation.

It seems clear that the hypothalamic centers are sensitized to receive the "message." However, the nature of the "messengers" is not clear. Brobeck has suggested that the hypothalamic centers may react to temperature changes produced by metabolism of the nutrients (22). The problem remains to be resolved.

To round out the picture of the feeding homeostatic mechanisms, one other feature must be described. If satiety results from the ingestion of "just enough" nutrient to maintain balance of intake versus energy output, then one might suppose that increased utilization of energy for growth, extra work, cold temperature, etc., would "divert" the energy intake and result in a lesser stimulus to the hypothalamic satiety center. This would result in an increased food intake until a new level of equilibrium was established.

This adaptive mechanism would take care of relatively acute challenges to homeostasis. There is apparently an additional adaptive mechanism which tends to maintain the constancy of the size of the fat depots. This is exemplified by the return to previous weight after a depleting illness. The mechanism is obscure. It is speculated that in some fashion the size of the fat depots influences the rate of fat metabolism and thus in turn affects the "satiety mechanism."

It is truly one of the great wonders of biology that the body weight remains so constant!

XUM

THE PATHOGENESIS OF OBESITY
or Why Does Everything I Eat Turn into Fat?

The person who is getting fat is eating more than he needs for growth, tissue repair and energy utilization. At which site may the homeostatic mechanism have broken down?

1. Destructive hypothalamic lesions in man have been described in which the patient had an "insatiable appetite" and presented progressive obesity. Such patients are uncommon, and one might expect other stigma of hypothalamic disease such as disturbances in temperature regulation and sleep pattern.

2. There is the purely speculative, intriguing possibility that certain individuals may be genetically endowed with "poorly tuned" or inadequate hypothalamic feeding centers. Such a person would have problems similar to those of the experimental animal with damaged hypothalamic "satiety" areas. Eating would tend to continue beyond "body needs" with accumulation of large fat depots, which in turn might act in some limiting fashion to help establish "equilibrium" at some outsize level. It almost seems fruitless to speculate along these lines until technics are developed to assay "satiety" and "food drive" in infants before learned behavior and conditioned eating patterns hopelessly complicate the problem. If there should happen to be such a disorder, the subject might control the tendency to obesity by an eating pattern limited by self-discipline. Should he become obese, the frustrations involved plus the complexities of living would result in a clinical picture probably considered obesity of psychogenic origin.

3. There are endocrine and metabolic disorders which warrant exploration as possible causal factors in obesity.

a) Thyroid deficiency was one time a fashionable explanation for obesity. However, according to the scheme outlined earlier, thyroid deficiency leading to lowered metabolic activity will result in decreased utilization of nutrients. Satiety should then occur after the ingestion of a decreased quantity of food. And, in fact, decreased food intake and lack of increased fat depots are characteristic of myxedema. Myxedema fluid accounts for the largest percentage of the excessive weight.

b) Cushing's syndrome, whether due to adrenal disease or to steroid administration, is characterized by extraordinary fat dep-

osition as to both location and quantity. The reason for the location of the excessive fat deposition in face, cervical hump and abdomen remains a fascinating mystery. From animal studies primarily, we know that neural factors have some control over the variously located fat depots. From observations of body contours in families, it is apparent that genetic factors have to do with patterns of fat storage. Also, it is patent that sex steroids influence localization of subcutaneous fat deposits. Perhaps further study of fatty tissue will solve some of these puzzles. For the present, there are no good insights into the mechanisms.

To return to the influence of hyperadrenocorticism on excessive fat deposition. Current studies have emphasized the role of the hypothalamus in the pituitary-adrenal axis. The evidence is purely inferential; however, there is a possibility that hypothalamic feeding control may be altered by the hyperadrenocortical state. A more reasonable likelihood has to do with the change in the "metabolic mixture" resulting from this endocrine disturbance. The over-all pattern is characterized primarily by decreased protein anabolism, impaired carbohydrate utilization and increased fat deposition as well as increased burning of fat. The picture is far from clear; however, the diversion of nutrients from the normal metabolic pathway may result in failure of satiety to occur at the usual level of food intake. It would appear that the obesity of Cushing's syndrome is unique: fat deposited in excess as the tissues are depleted of protein. It is hardly likely that the pathogenesis of "ordinary" obesity follows this course in the absence of stigmas of hyperadrenocorticism.

There is a variety of genetic obesity in the mouse characterized by an obscure, metabolic defect in which there is an augmented tendency to fat deposition. The hypothalamic mechanisms appear to be intact. There is no recognizable human counterpart of this disorder; however, its clarification may offer considerable insight into the problem in man.

c) Hyperinsulinism due to an islet cell tumor produces hypoglycemic episodes which are frequently characterized by hunger sensations. The patient may overeat in response to this stimulus, or he may overeat deliberately when he learns that frequent carbohydrate ingestion may prevent or abort hypoglycemic attacks. Islet cell tumors are relatively uncommon. So-called functional hypoglycemia thought to be due to overresponsiveness of the

insulin release mechanisms is more commonly seen; this disorder is not characterized by a tendency to obesity. Nor, in fact, do obese individuals show a tendency to hypoglycemia.

As mentioned earlier, whereas excessive insulin resulting in hypoglycemia may produce a sensation of hunger, the daily variations in hunger and satiety have not been unequivocally related to blood sugar levels or A-V differences.

d) The gonadal hormones have been implicated in the obesity problem mainly in relation to the castrate. However, the effects of castration in man and in the experimental animal are inconstant in this regard. There is no doubt that the female sex steroids favor fat deposition in characteristic areas. This is illustrated well by the changes at puberty. It is perhaps more dramatically shown in the disappearance of these fat deposits in the virilized female. The mechanisms of this antagonism are not known. The anabolic effects of the male sex hormones far outweigh those of the female hormones. The "metabolic mixture" is altered to favor protein formation and muscle building. The prepubertal fat boy, who suddenly starts to grow and loses his fat, is thought to exemplify this type of effect.

There is a tendency to accumulate fat with the passage of years. Even as the weight remains constant, fat comes to represent a higher proportion of the body weight (1). It is not known whether this represents primarily a disparity between a falling off in energy utilization with a frozen habit pattern of intake or whether the changing hormonal pattern is an important feature. The ovariectomized rat and mouse offer fascinating clues, when one speculates in particular about the postmenopausal woman. Following castration of the rodents their spontaneous activity is markedly depressed, the food intake does not fall off commensurately and they gain weight (23). We apply the clues, not the conclusions, to man.

The role of the sex steroids seems important and warrants further elucidation.

4. Psychogenic factors are widely held to be the primary influence in the production of obesity. This concept offers a reasonable working approach to the clinical problem. The proof, as is true of so many reputed psychogenic disorders, is far from rigid. The life experience of an individual, especially in infancy and childhood, results in countless influences affecting eating behavior.

XUM

One does not need psychiatric insight to appreciate that the infant derives pleasure from being fed when hungry. There is relief of the restlessness and abdominal discomfort. The overactive hungry mouse or rat decreases activity to exceedingly low levels after refeeding. And anyone who has fallen asleep at a 2 o'clock afternoon lecture will attest to the sedating effect of food.

Psychiatrists have offered interpretations of the emotional and symbolic overtones involved in the offering and receiving of food by parents and infants respectively. In essence it is suggested that food begins to stand for love and protection as well as a nutrient. The neurotic parent may urge food on the infant because of an inability to express affection. The infant, for his part, may take food in his unavailing search for emotional sustenance. In addition, it is postulated that "oral aggressive drives" may be expressed in eating and that eating, in turn, may come to represent an expression or outlet of hostile feelings. It is not proposed to review the various psychiatric interpretations of the psychodynamics of obesity; there is common agreement that overeating represents neurotic behavior. The individual with this disorder "eats to satisfy some emotional need." The obese body image is thought to take on profound symbolic significance. The homeostatic mechanisms ordinarily controlling food drive and satiety are overwhelmed by higher centers, and the nice balance between energy requirements and food intake is disturbed. On one hand, obesity may result; on the other, various degrees of inanition may result from psychogenic aversion for food, or anorexia nervosa.

In general, these concepts have been derived from study of obese children and their families and from intensive psychiatric studies of selected obese patients. By and large they are supported by the experience of the physician who attempts to treat obese patients and is impressed with the chronic nature of the disorder, the extraordinary cravings uncovered, the concealments and fabrications (similar to those of the alcoholic) and, among other things, the depressions and anxieties apparently related to the dietary restrictions.

5. Bad eating habits may be considered an explanation for obesity along lines similar to the preceding category, but without the neurotic overtones. It is not unreasonable to assume that cultural or family patterns of eating may become so fixed as to overwhelm the homeostatic controls of food and energy balance.

XUM

In this category may be included episodes of excessive fat deposition (in contrast to the situations above in which there is a sustained disruption of homeostasis and a continuing tendency to put on fat). Such episodes would include lag periods in life when activity has diminished, energy requirements have fallen off, yet the habit of heavy eating is maintained for a while, with resultant fat accumulation. Psychologic factors undoubtedly add to the complexity of evaluating these periods of change; however, one may consider such an example as going from vigorous college athletics or heavy manual work to a sedentary job. Perhaps the farmer's tendency to gain weight each winter illustrates this mechanism.

6. False concepts. It is proper to enumerate the postulations concerning unique features of the obese individual which have never been substantiated: increased absorption, increased utilization, smaller than normal specific dynamic action of food, a defect in over-all energy metabolism, and inability to mobilize fat stores. All of these concepts have been studied by Newburg (24) and others (9, 25–27) and shown to have no scientific or physiologic basis to differentiate the obese from the normal individual.

THE TREATMENT OF OBESITY

or Can't I Take a Pill or Something?

The treatment of the hyperphagia which has led to obesity is quite unsatisfactory, to say the least. A starvation program is unpleasant for anyone, especially, one might suspect, for the fat man. Unfortunately the pleasures of satiety are apparently not derived from burning one's own fat stores. Therefore, voluntary starvation for long periods of time will be successful only when there is a high degree of sustained motivation.

The selection of patients for the management of obesity is a critical feature of the problem, as some patients may be made worse by a starvation regime.

We might first consider the personality of the patient, as several excellent articles have stressed the importance of emotional factors (28–32). We have discussed the concept that a disturbance of homeostasis manifested by hyperphagia may result in obesity. This is a reasonable concept and a working hypothesis. What we, as physicians not trained in psychiatric technics, will

XUM

be able to do to evaluate the patient and help him to regain control of food intake is difficult to define. It is important to find out if the patient really wants to lose weight and why. So many obese patients have not asked to be reduced but are "being reduced" by their physicians because of some associated pathologic condition or as a preventive measure.

In a series of office visits over a few weeks it is usually possible to evaluate the motivation to some extent and perhaps some of the conflicts which seem to be a factor in the inability to control food intake. It has been suggested (29) that such patients be evaluated and an attempt made to place them in one of the following categories: (1) overeating as a response to nonspecific emotional stress; (2) overeating as a substitute gratification to intolerable life situations; (3) overeating as a symptom of an underlying emotional illness, especially depressions and hysteria, and (4) overeating as an addiction to food. This is an excellent outline, and probably such classification should be attempted, but it is not a simple matter to ascertain the group in which the patient belongs. This classification based on psychodynamics represents patients with rather severe emotional problems. In our experience this would include the markedly obese children and the adults with numerous functional complaints who have always been obese and are not interested in weight reduction. Unfortunately the latter constitute a large majority of an office or clinic practice. The results with this group are very disappointing as judged by weight reduction. How to pick out the patients in this group who should not be placed on a reduction diet is difficult. It is mentioned frequently that if the emotional cause of the obesity is not found and removed the hyperphagia will continue. This may be true, but finding the cause is difficult, and it may turn out that one neurotic mechanism supersedes another without much clarification of causes. And, in fact, patients have been known to get well without benefit of insight.

There is one group of patients which is easier to motivate and in which the psychiatric factors seem less prominent. First is the patient with a serious illness such as diabetes mellitus, myocardial infarction or osteoarthritis. Oftentimes a discussion of the benefits of weight reduction is sufficient to stimulate such a patient to undertake a reducing regime. The middle-aged man with a "spread" may ask for a reducing regime because he has read of

the hazards of obesity. The patient who believes she is fat because "mother was fat" can be re-educated regarding eating habits. There are other examples, but the point to be made is that this group can be motivated because they are uncomfortable enough with the extra weight to attempt weight reduction or weight reduction offers them hope of alleviating or preventing further serious illness.

What constitutes a positive working approach to the obese patient if one believes that emotional factors play a large role in causing hyperphagia?

First of all, as with any type of medical problem, an adequate history is imperative. To be stressed are early development, eating pattern of the family, weights of other members of the family, age of onset of obesity, pattern of reaction to traumatic situations, sexual and social adjustment, reason for consulting a physician and the motivation for attempting weight reduction. To obtain this type of history may require several office visits.

After obtaining a history and completing the physical examination, one attempts to evaluate the seriousness of the emotional problem. It seems clear that a reduction regime may prove harmful in precariously adjusted individuals and should not be attempted (33).

Obviously if overeating represents a neurotic adjustment, the answer is to cure the neurosis. We have not been able to accomplish this and are unaware of any convincing reports in the literature. The next best thing would be to find a substitute for food which is being used to allay the anxieties. Support, reassurance and interpretation of the patient's problems seems to be a much better substitute than scolding or frightening. However, our experience has been that many obese patients keep their appointments for four to six months and then disappear. The fact that the patients do not return suggests to us that attempted weight reduction has upset an emotional balance which the patient has maintained by overeating. This is consciously or unconsciously recognized by the patient and he does not return for further therapy. The psychologic approach seems to be the best method at the present time, but the results are discouraging.

After selecting the patients who are to be placed on a reduction regime we might first discuss the type of diet to be used. A review of the literature reveals innumerable papers on the dietary

XUM

treatment of obesity. What can one deduce from all this mass of information? We should like to know (1) the range of calories, (2) the type of food mixture which is best, e.g., high protein, low fat or high fat, low carbohydrate, (3) the value of anorexogenic drugs and/or thyroid substance, and (4) complications or problems of a reduction regimen.

It has been shown that an obese patient requires between 20 and 24 calories per kilogram per day to maintain his weight on normal mixed diets (7). This means that a person weighing 230 lb. (100 kg.) requires 2,000–2,400 calories per day to maintain his weight. This figure is the basal caloric requirement and is probably low. It has been reported that two hospitalized obese patients lost weight on a diet containing 2,800 calories, and it was calculated that their previous intake had probably been over 4,000 calories (34). These figures highlight the fact that the obese person who states that he "eats like a bird" must have a poor memory. They also mean that an obese person will lose weight on a diet containing between 800 and 1,200 calories. It has been our practice to prescribe an 800 calorie diet so that a rather rapid weight loss will take place. This encourages the patient and he is more likely to follow the reduction regimen. However, the degree of food restriction should not be rigid in all patients. Some patients do very well if allowed to choose their own restricted diet and are given only support and reassurance. Reported studies indicate that it is possible to reduce the caloric intake to 450 calories and still maintain nitrogen equilibrium (27). These studies also confirm the fact that an obese person with a caloric deficit has no difficulty mobilizing the body fat as a source of energy. A nonobese patient on this regime will be in negative nitrogen balance because he has no fat stores to call on as a source of energy (35). It is customary to prescribe added vitamins with this low calorie diet.

The type of diet to be prescribed as regards proportion of food stuffs is somewhat controversial. When prescribing an 800 caloric diet we have tended to make it high in protein because it has been our impression that the patients were less hungry on this type than on a low or average protein diet. A recent study (20) showing a higher satiety value of an 1,800 calorie diet containing 116 Gm. of protein over an isocaloric diet containing 35 Gm. of protein tends to confirm this impression.

Another reason for prescribing a high protein diet is to take advantage of the specific dynamic action of protein. The rise in heat production which follows the ingestion of foods has been called "the specific dynamic action." It is greatest for protein, less for carbohydrate and least for fat. It has been called "the cost of digestion." It has been estimated that on a diet of average protein intake, about 10 per cent of the protein is used to meet the specific dynamic action. As the content of protein in the diet reaches high levels, two or three times this amount may be used (36), and for this reason it seemed logical to take advantage of this fact to help produce a caloric deficit.

Dole *et al.* (37) in an excellent study have presented evidence that the content of protein in the diet seems to determine the appetite. Their patients were required to eat a basic diet containing 35 Gm. or less of protein and were allowed calories ad libitum as carbohydrates and fats. The protein content of the diet was increased by the addition of a rather unpalatable supplement. As the protein content was increased, there was a voluntary increase in caloric consumption. This was interpreted to be the result of an increase in appetite. These workers offer the interesting interpretation that the effect of a low dietary supply of protein leads to a reduction in metabolic activity of proteins and associated metabolites. Any change in the rate of one process would change the inventory of metabolites that are shared with other rate processes. "Because of the imbalance of rates, some of the other metabolites come to be in relative surplus. The appetite, therefore, is depressed and the inventory of the other metabolites is allowed to shrink until a new steady state is reached, a matter of several months in case of protein restriction." This is a very attractive hypothesis and offers a new approach in investigating human appetite. It also suggests that the prescription of a *high* protein diet may stimulate the appetite rather than produce satiety. Dole's patients on the low protein diet did not admit to hunger or weakness.

A word of caution regarding the use of a low protein diet on a large scale. Dole and his associates did not find any evidence of deficiency symptoms, but this might be expected from previous knowledge of protein needs.

A high fat, high protein, low carbohydrate diet has been recommended in the treatment of obesity (38). One gets the

XUM

impression that this diet is believed to produce its benefit without decreasing caloric intake. This has been shown not to be the case in careful studies that disclosed no demonstrable difference in weight reduction on a high fat diet compared to an isocaloric high carbohydrate diet (34). Any result from this diet therefore must be due to a decrease in appetite and hence caloric intake.

The prescription of a diet which the patient does not like or which is radically different from his previous diet will probably be a reducing diet provided the patient does not eat other foods. Weight reduction will take place because there is a voluntary decrease in food intake. However, the long term therapy of obesity with an unpalatable diet will not be successful. Success will result only when a diet is found that is acceptable to the majority of obese patients and will provide a caloric deficit. We do not have this diet at the present time.

Finally we would like to stress that, to be significant, any study on a method of weight reduction must have been carried out over at least one year. It has been our impression that any study of only six months' duration will look good. This is because most patients will diet for about this length of time and then return to their former eating pattern. For this reason any new crutch recommended as an aid for dieting must have a long term follow-up before its value is considered proved.

A few general remarks about dietary management may be helpful. It is a common observation that a large percentage of obese patients have a characteristic eating pattern. "I have a cup of coffee *without sugar* for breakfast, a sandwich and a small glass of milk for lunch, and I have my big meal for dinner." We have no explanation for this rather common eating pattern but feel that it is probably best to suggest a more normal distribution of food intake as part of the dietary training program.

It is well to point out to patients that weight reduction may not begin immediately after the institution of the diet. The studies of Newburg (24) show very clearly that there may be a period of water retention and hence no loss of weight for as long as 18 days after institution of the low calorie diet. This phenomenon is unexplained, but it should be mentioned to the patient. It is during these first few days that the patient is hungry and discouraged. The failure to lose weight will add to

his discouragement unless he is aware that the period of water retention is followed by diuresis and the expected weight loss.

Anorexogenic drugs and thyroid substance are commonly prescribed in conjunction with the low calorie diet. The use of sympathomimetic drugs as appetite depressants began following the observation that weight reduction occurred as a side effect in patients receiving amphetamine for mood disturbances (39). Soon after that they were introduced as anorexogenic drugs in the treatment of obesity (40). Since the first report in 1938, innumerable papers have appeared on the value or lack of value of these drugs; about 65 per cent of patients treated for obesity are said to receive some type of anorexogenic drug (41).

A recent editorial (42) states: "No drug has yet been discovered that will safely and effectively control the appetite but that one may yet appear is certainly possible." This is the philosophy that we have used in the management of obese patients. In short term studies of four to six months, amphetamine has seemed to be of value in depressing the appetite (43). Long term studies (44) have shown that diet alone compares favorably with results obtained with diet and amphetamine. Habituation and toxicity have followed the use of such drugs (44), so their indiscriminate use is to be condemned. The use of the anorexogenic drugs may prevent the patient from facing the fact that permanent results can be obtained only by reducing food intake and by no other means.

Thyroid substance has been used for many years as an aid to losing weight. It was thought that the metabolic rate could be increased and hence "burn more fat." Recent studies have conclusively shown that this is not the case, as endogenous thyroid function decreases as exogenous thyroid is administered (45). The end-result is that the metabolic rate is not increased and the patient has a false sense of security in thinking that he can continue to eat large quantities because the thyroid will burn up the excess food. Most patients are started on thyroid substance because of a low BMR, which is common in the obese state. It is worth emphasizing that this does not necessarily mean hypothyroidism but rather that oxygen consumption in terms of the large surface area is low. Actually the total oxygen consumption may indicate an increased metabolic load. The obese patient derives no benefit from thyroid therapy, whereas the

XUM

patient with hypothyroidism will respond dramatically to 15–30 mg. Several studies have shown that thyroid therapy is of no value in obesity unless there is hypothyroidism (46).

We need to continue our search for a better understanding of the mechanisms of hyperphagia and a more satisfactory reducing regime. A five year follow-up of 294 patients under treatment for obesity revealed that only 193 were available for follow-up. Of the latter group, 21 per cent continued to show weight loss. This would be only 14 per cent of the original group (47). The experience at the Washington University Clinics is in line with our own (48). Eight hundred and seventy low calorie diets were prescribed in a one year period; 548 patients did not return for re-evaluation, and only 24 patients even maintained contact with the clinic for a period of 25–52 weeks. Group psychotherapy patterned along the lines of Alcoholics Anonymous has been tried with poor results (49).

In attempting to give support to the patient, one does well to remember that reducing is a hard, long drawn out regime associated with frustrations, mental torture and, most of all, with hunger contractions. Each case must be individualized, and the physician must be willing to take time to establish a close doctor-patient relationship, because the prescription of the diet is only a small part of the treatment. Even though the percentage of success is low, the occasional success is enough to maintain one's enthusiasm to continue until better methods are available.

SUMMARY

1. Obesity in man is a disease of unknown etiology. It is associated with decreased longevity and increased morbidity, both of which can be altered by a reduction in weight.

2. Experimental studies in animals have been reviewed. The central nervous system appears to play an important role in the control of food intake in animals. These studies, which are extremely interesting, cannot be applied directly to man until adequate devices are available to measure "food drive" and "satiety" in the human being.

3. In the obese patient, psychologic factors seem to play a large part in the loss of control of food intake. These factors are difficult to evaluate and even more difficult to quantitate.

4. A diet which produces a "calorie deficit" is still the only way to produce weight reduction. The results of diet therapy are discouraging even when combined with an attempt to understand the underlying psychologic factors disturbing homeostasis.

5. The poor results in the treatment of obesity should act as a stimulus to continued research in this field.

APPENDIX

DIET THERAPY

by SARAH BRENT, B.S.

There are numerous theories regarding the dietary level most satisfactory for ambulatory patients. It has been our experience that, initially, an 800 calorie diet containing adequate protein is acceptable to most patients. This diet not only produces a good weight loss but is often as satisfying as those of slightly higher caloric levels—1,000–1,400 calories. Needless to say, dieting is difficult; the patient must understand this, and that maintenance of normal weight, once it is reached, will require continued re-education of former eating patterns. The former overweight individual must constantly be on guard against regaining lost weight.

The 800 calorie diet is made up basically of lean meat, fish or poultry, eggs, cheese, low carbohydrate vegetables, unsweetened fruits and juices, a small bread allowance and skim milk. A suggested outline of an 800 calorie diet follows.

Breakfast:

1 serving fruit or juice
2 eggs or small serving of lean meat (2 oz.)
1 slice of bread
Coffee or tea as desired without cream or sugar

Lunch or Supper:

1 small serving lean meat, fish or poultry or meat substitute (1 oz.)
1 cup Group I vegetable
1 serving fruit
1 cup skim milk
Coffee or tea as desired without cream or sugar

Dinner (main meal):

1 average serving lean meat, fish or poultry (3 oz.)
1 cup Group I vegetable

XUM

½ cup Group II vegetable
1 serving fruit
1 cup skim milk
Coffee or tea as desired without cream or sugar

MEATS, FISH, AND POULTRY ALLOWED:

1. Meats should be boiled, baked or broiled and should be trimmed of all visible fat. Those allowed are: beef, chicken, turkey, veal, lamb, pork, white fish (as haddock, cod, halibut), shrimp, clams, oysters, liver.

Substitutes that may be used for meat include:

Eggs, 1=1 oz. meat; cheddar cheese, 1 slice=1 oz. meat; cottage cheese, dry, ¼ cup=1 oz. meat; peanut butter, 2 scant tablespoons= 1 oz. meat; cold cuts as bologna, spiced ham and salami, 1 slice=1 oz. meat.

VEGETABLES (raw or cooked in plain salted water):

Group I. Up to 2 cups daily (can be mixture of several)

Asparagus	Eggplant	Sauerkraut
Chicory	Greens, any kind	String beans
Broccoli	Lettuce	Summer squash
Brussels sprouts	Parsley	Tomatoes
Cauliflower	Okra	Watercress
Celery	Green pepper	
Cucumbers	Radishes	

Group II. ½ cup daily

Carrots	Peas	Pumpkin
Beets	Onions	Turnip

Small amounts of vinegar or lemon juice are valuable in improving the taste of vegetables.

FRUITS AND FRUIT JUICES:

1. Fresh, cooked or canned without sugar.
2. The diet should include 1 serving of orange, grapefruit or tomato juice (or tomatoes) daily, as part of fruit allowance.

	Amount to Use
Apple (2" diameter)	1 small
Applesauce	½ cup
Apricots, fresh	2 medium
Apricots, dried	4 halves
Banana	½ small
Blackberries	1 cup
Blueberries	⅔ cup
Cantaloupe (6" diameter)	¼
Cherries	10 large
Dates	2
Figs, fresh	2 large

	Amount to Use
Figs, dried	1 small
Grapefruit	½ small
Grapefruit juice	½ cup
Grapes	12
Grape juice	¼ cup
Honeydew melon, medium	⅛
Mango	½ small
Orange	1 small
Orange juice	½ cup
Papaya	⅓ medium
Peach	1 medium
Pear	1 small
Pineapple	½ cup
Pineapple juice	⅓ cup
Plums	2 medium
Prunes, dried	2 medium
Raisins	2 tablespoons
Raspberries	1 cup
Strawberries	1 cup
Tangerine	1 large
Watermelon	1 cup
Tomato Juice	1 cup

MILK:

1. The diet should include milk, as skim, skim buttermilk or skim milk powder daily.

1 cup skim milk=1 cup skim buttermilk=¼ cup skim milk powder

This milk may be used for drinking or in cooking. Some dieters find that drinking the milk between meals helps allay feelings of hunger and protects them from eating other foods.

Obese patients belonging to the "nibble" group derive satisfaction from between-meal snacks of no-calorie foods or beverages. The following may be taken as desired:

Black coffee or tea without cream or sugar.

Fat free broths and bouillon.

Lemon or lime juice; use artificial sweetener, as saccharine.

Plain gelatin flavored with lemon or lime juice and sweetened with artificial sweetener.

Pickle, unsweetened, as dill.

Cranberries and rhubarb, cooked; use artificial sweetener.

Rennet tablets combined with part of milk allowance to make junket.

The common complaint of such a diet as this is its simplicity. The dietitian plays an important role in suggesting combinations of the foods allowed, because one soon tires of plain meat, plain vegetables, plain fruits, etc. Combinations, as tossed salad with a no-calorie dress-

XUM

ing, made of tomato juice plus various spices and seasonings, and fruit added to the plain gelatin, are permissible. There is no objection to mixtures of foods as long as the patient does not exceed his own daily allowance.

A vitamin supplement (multivitamins) is suggested in order to insure daily adequacy. We have found no cause to restrict the intake of salt or water in the treatment of uncomplicated obesity.

Again, dieting is difficult and the willing patient will need continued reassurance and support from the dietitian as well as from the physician.

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XUM

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